2010 Annual Report: iPS Cells

News at CIRM

Unraveling the Role of iPS Cells

In the three years since scientists successfully turned back the clock on human adult skin cells, CIRM researchers have been working to make these reprogrammed cells—called induced pluripotent stem (iPS) cells—a safe and effective counterpart to embryonic stem cells. As CIRM scientists improve techniques for creating the flexible cells, they are discovering that iPS cells do not behave—for better or for worse—exactly like their embryonic counterparts.

Making a Better iPS Cell

Since 2006, when Shinya Yamanaka of the Gladstone Institutes and Kyoto University first reprogrammed human skin back to an embryonic-like state, stem cell scientists have been scurrying to improve on the technique in humans.

The problem was that despite the cells' obvious usefulness in understanding and possibly treating disease, creating them involved permanently inserting cancer-causing gene. Plus, techniques to generate the cells were extremely inefficient.

Papers quickly began appearing demonstrating that the number of genes needed has been whittled down and that the efficiency has improved, with 2010 bringing significant advances by CIRM grantees.

In February, CIRM grantees at Stanford University discovered a way to transform fat cells into iPS cells without requiring viruses.

"This technique is not only safer, it's relatively simple," Michael Longaker, Stanford University professor of surgery, said in a press release. Longaker is a co-author of the study that appeared in Nature Methods in February.

The team used so-called minicircles of DNA to reprogram the cells into pluripotency. These minicircles contain just the four genes needed to transform the cells, along with a fluorescence gene that allows the cells to be tracked. The minicircles are about half the size of naturally occurring DNA rings called plasmids that have been used in other iPS transformations, and unlike integrating viruses, the minicircles are lost over time along with the potentially dangerous reprogramming genes, making the cells safer for therapy.

The idea, said Stanford cardiologist Joseph Wu, is to one day take a fat or skin biopsy from a member of a family with heart problems, reprogram the cells and make cardiac cells to study in a lab dish. Wu, the senior author of the study, notes: "This would be much easier and less invasive than taking cell samples from a patient's heart."

Later in the year a team at Harvard University developed another method for virus-free creation of iPS cells. In that work, the scientists used transient RNA in a technique that also appears to be much more efficient than previous techniques.

Modeling Disease-in-a-Dish

Despite concerns about genetic anomalies in iPS cells, (see sidebar) they are proving valuable in understanding the origin of diseases. CIRM grantees have taken skin samples from people with genetic forms of autism, premature aging, Parkinson's disease and schizophrenia, reprogrammed them into iPS cells and matured those into the affected cell type. The resulting cells have provided a first glimpse of what might be happening at the cellular level in those conditions.

Take Parkinson's disease, for example. Work by CIRM grantees at Stanford University and The Parkinson's Institute has led to neurons in a lab dish that exhibit signs of the disease. The cells, matured from iPS cells created from a woman with a genetic form of Parkinson's disease, produce excess protein that is a hallmark of the disease and also show signs of a form of cellular stress associated with Parkinson's disease.

In addition to providing insights into a disease, these models can be used for the first time to screen for drugs that halt or reverse disease symptoms in human cells.

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